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Antimicrobial susceptibility of *Streptococcus pneumoniae* in Latin America: results from five years of the SENTRY Antimicrobial Surveillance Program

M. Castanheira[1], A. C. Gales[1], R. E. Mendes[1], R. N. Jones[2] and H. S. Sader[1,2]

[1]Laboratório Especial de Microbiologia Clínica, Disciplina de Doenças Infecciosas e Parasitárias, Universidade Federal de São Paulo, São Paulo, Brazil and [2]The Jones Group/JMI Laboratories, North Liberty, IA, USA

ABSTRACT

A total of 1561 pneumococcal isolates were collected in 1997–2001, mainly from patients with community-acquired respiratory tract infections, and susceptibilities were tested by reference broth microdilution against 29 antimicrobial agents. In general, 69.3% of strains were considered susceptible (MIC ≤ 0.06 mg/L) to penicillin. Resistance to penicillin (MIC ≥ 2 mg/L) and cefotaxime (MIC ≥ 4 mg/L) was found in 11.9% and 0.4% of isolates, respectively. The fluoroquinolones gatifloxacin (MIC_{90}, 0.5 mg/L) and levofloxacin (MIC_{90}, 1 mg/L) were active against >99% of the isolates tested. Among the other non-β-lactam drugs tested, the rank order of susceptibility was chloramphenicol (95.6%) > clindamycin (94.5%) > azithromycin (88.5%) > clarithromycin (87.5%) > tetracycline (79.5%) > trimethoprim + sulphamethoxazole (60.5%). The penicillin-non-susceptible isolates presented higher rates of resistance to other antimicrobial agents. The rank order of penicillin resistance rates among the seven participating countries was Mexico (25.0%) > Uruguay (19.2%) > Chile (18.3%) > Colombia = Argentina (9.9%) > Brazil (3.9%) > Venezuela (2.8%). The regional rate of penicillin resistance did not vary significantly over the years studied (p 0.339). Screening for the *ermB* and *mefA* genes by multiplex rapid cycle PCR on 23 erythromycin-resistant isolates collected during the year 2001 showed that 43.5% and 56.5%, respectively, were positive for *ermB* and *mefA*. Overall, the results indicated that antimicrobial susceptibilities of *Streptococcus pneumoniae* vary significantly among Latin American countries. Regional and local surveillance programmes are necessary to guide empirical therapy of pneumococcal infection in Latin American countries.

Keywords Community-acquired pneumonia, fluoroquinolones, Latin America, respiratory tract infections, SENTRY, *Streptococcus pneumoniae*

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INTRODUCTION

Streptococcus pneumoniae remains a major cause of morbidity and mortality in humans. This pathogen accounts for most cases of community-acquired pneumonia and other respiratory infections. In addition, it is a leading cause of meningitis, particularly in adults, and acute otitis media in children. During the past 30 years, pneumococci have developed resistance to several antimicrobial agents, including penicillin, tetracycline, trimethoprim + sulphamethoxazole, chloramphenicol, erythromycin and cephalosporins [1].

The emergence and worldwide dissemination of penicillin resistance among *S. pneumoniae* strains represents an important problem in the treatment of respiratory tract infections [2,3]. Infections caused by penicillin-non-susceptible strains may be treated intravenously with third-generation cephalosporins. However, there are very few options available to treat infections, especially meningitis, caused by strains resistant to third-generation cephalosporins, since glycopeptides do not penetrate well into the central nervous system. In addition, the fluoroquinolones,

Corresponding author and reprint requests: H. S. Sader, The Jones Group/JMI Laboratories, 345 Beaver Kreek Centre, Suite A, North Liberty, IA 52317, USA
E-mail: helio-sader@jmilabs.com

which remain very active against multiresistant pneumococci, have not yet been approved for use in children [1,4].

Since pneumococcal infections are usually treated empirically and the susceptibility patterns are not predictable, surveillance programmes are necessary to guide antimicrobial therapy. The SENTRY Antimicrobial Surveillance Program was established in 1997 to monitor antimicrobial resistance patterns of nosocomial and community-acquired infections via national and international networks of sentinel medical centres. The aim of this study was to evaluate and compare antimicrobial resistance rates among *S. pneumoniae* isolates from Latin American countries during 1997–2001.

MATERIALS AND METHODS

Bacterial strains

In total, 1561 *S. pneumoniae* isolates collected consecutively by the participating clinical microbiology laboratories from January 1997 to December 2001 were evaluated. Only isolates judged to be the cause of defined community-acquired respiratory infections were included in the study. Respiratory tract specimens included high-quality sputum, tracheal aspirate and bronchoalveolar lavage. Only specimens with high numbers of macrophages and low numbers of epithelial cells were accepted [5]. Strains isolated from the blood of patients with community-acquired respiratory tract infections were also included in the study.

Ten Latin American laboratories participated in the study each year. The laboratories were in six countries (nine cities): Sao Paulo, Rio de Janeiro, Florianopolis, Porto Alegre and Brasilia, Brazil; Buenos Aires and San Isidro, Argentina; Santiago (two centres), Chile; Medellin, Colombia; Mexico City, Mexico; and Montevideo, Uruguay. In 1998, the Montevideo centre was replaced by a centre in Caracas, Venezuela, and in 1999, the Brazilian centre located in Rio de Janeiro was replaced by a centre in Porto Alegre, which is also located in the southern region of Brazil. In 2001, the centre located in Medellin, Colombia was replaced by a centre located in Brasilia, Brazil. The selection of centres was based on the principle that they should be sentinels for their respective geographical regions. All isolates were saved on agar slants and sent to the monitoring centre for storage and further characterisation by reference identification and susceptibility testing methods. Erythromycin-resistant isolates collected during the year 2001 were selected randomly and screened for the *ermB* and *mefA* genes [6].

Species identification

The isolates were identified at the participating centre by the routine methodology used at each laboratory. Upon receipt at the monitoring laboratory, the isolates were subcultured on blood agar to ensure viability and purity. Species identification was confirmed or performed with the Vitek system (bioMérieux, Hazelwood, MO, USA) or API (bioMérieux) products and standard reference methods [7]. Isolates were frozen at −70°C until they were processed.

Susceptibility testing

Antimicrobial susceptibility testing of isolates was performed by reference broth microdilution methods [8]. Antimicrobial agents were obtained from their respective manufacturers. Quality control was performed by testing *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *S. pneumoniae* ATCC 49619, and *Enterococcus faecalis* ATCC 29212. Interpretive criteria for each antimicrobial agent tested were as published previously [9]. Rates of susceptibility to cefotaxime were calculated according to the breakpoints for non-meningitis isolates (≤ 1 mg/L) [9].

Molecular analysis

Screening for *ermB* and *mefA* was performed by multiplex rapid cycle PCR as described by Farrell *et al.* [6]. Molecular characterisation of the quinolone resistance-determining region was performed by PCR amplification of the *gyrA*, *gyrB*, *parC* and *parE* genes, followed by sequencing of the amplicons as described previously [10].

Statistical analysis

Data were analysed with SPSS for Windows Release 10.0.5–Standard Version (SPSS Inc., Chicago, IL, USA). Fisher's exact test and χ^2 for trend were used to compare proportional differences for penicillin-resistant *S. pneumoniae* isolates among periods and regions. Differences were considered statistically significant at a p value of < 0.05.

RESULTS

The isolates were collected either from the respiratory tract (77%) or blood (23%), with 33% of patients hospitalised at the time the specimen was collected. Patient age data were not available for *c.* 50% of the cases. However, where ages were known, the distribution was as follows: ≤5 years, 27.7%; 6–20 years, 8.5%; 21–40 years, 15.8%; 41–64 years, 24.1%; and ≥65 years, 24%.

The in-vitro activities of selected antimicrobial agents tested against the *S. pneumoniae* isolates are summarised in Table 1. Among 1561 strains evaluated, 69.3% were susceptible to penicillin (MIC ≤ 0.06 mg/L), 18.8% were intermediate (MIC of 0.12–1 mg/L), and 11.9% had high-level resistance (MIC ≥ 2 mg/L). An analysis of penicillin resistance rates (MIC ≥ 2 mg/L) according to age group showed that the highest rate was detected in children aged ≤5 years (15.6%), followed by the 41–60-year group (15.5%), the ≥65-year group (11.3%), the 21–40-year group

Table 1. In-vitro antimicrobial susceptibilities of *Streptococcus pneumoniae* isolates from Latin American hospitals participating in the SENTRY Antimicrobial Surveillance Program (1997–2001; 1561 strains)

	Cumulative percentage inhibited at indicated concentration (mg/L)[a]										
Antimicrobial agent	**≤ 0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**	**16**	**32**
Penicillin	60.7	**69.3**	77.1	82.3	85.1	88.1	95.6	99.6	> 99.9[b]	–	–
Amoxycillin	–	74.9	80.7	83.7	85.6	90.8	**98.2**	99.6	> 99.9[b]	–	–
Cefuroxime[b]	–	60.8	69.7	74.7	81.3	**84.5**	86.9	93.5	99.7[b]	–	–
Cefprozil	–	–	29.0	62.7	74.7	81.6	**84.1**	86.8	92.7	98.4[b]	–
Cefpodoxime	54.2	70.1	76.2	81.2	**84.4**	87.3	96.5	99.6	100.0[b]	–	–
Cefotaxime[c]	63.8	72.8	79.1	84.3	89.5	**98.3**	99.6	99.9	> 99.9[b]	–	–
Cefepime	–	72.5	77.9	82.8	87.1	**97.5**	99.7	99.8	> 99.9[b]	–	–
Erythromycin	–	–	–	**87.1**	88.1	89.5	91.2	93.1	95.0	96.2	96.4[b]
Azithromycin	–	–	86.1	87.0	**88.5**	89.4	91.1	92.3	93.8	94.7[b]	–
Clarithromycin	–	–	–	**87.5**	89.3	90.4	92.3	94.1	95.2	95.4	95.6[b]
Clindamycin	–	–	–	**94.5**	94.6	94.7	96.0	100.0	100.0[b]	–	–
Gatifloxacin	0.5	0.9	8.2	78.0	99.4	**99.7**	99.8	99.8[b]		–	–
Levofloxacin	–	–	–	–	30.7	94.2	99.8	99.8[b]	–	–	–
Chloramphenicol	–	–	–	–	–	–	71.0	**95.6**	96.8	99.3[b]	–
Tetracycline	–	–	–	–	–	–	**79.5**	81.0	82.8	89.1[b]	–
Trimethoprim + sulphamethoxazole	–	–	–	–	**60.5**	65.9	–	–	–	–	–
Quinupristin + dalfopristin	–	–	–	34.9	95.5	**100.0**	–	–	–	–	–
Vancomycin	–	–	4.5	53.9	98.9	**100.0**	–	–	–	–	–

[a]Interpreted by criteria for non-meningitis isolates [9]. The values in bold represent the percentages of susceptible strains.
[b]Percentage inhibited at the highest dilution tested.
[c]Percentage of susceptibility defined by cefuroxime axetil (oral) [9].
[d]Also indicates susceptibility spectrum of ceftriaxone [9].

(7.3%) and the 6–20-year group (3.4%). The penicillin MIC distribution among the isolates from patients whose ages were not known was very similar to that of the entire collection (data not shown).

Based on susceptibility breakpoints established in 2003 for non-meningitis isolates [9], cefotaxime resistance was found in only 0.4% of the total isolates. Amoxycillin (MIC_{90}, 1 mg/L) was active against 98.2% of isolates, while the fluoroquinolones gatifloxacin (MIC_{90}, 0.5 mg/L) and levofloxacin (MIC_{90}, 1 mg/L) inhibited 99.8% of the isolates at the susceptible breakpoints. Only three fluoroquinolone-resistant isolates were identified in the entire collection; these were isolated from the lower respiratory tract of adults. Two of these were isolated in Argentina in 1999 and the other was isolated in Chile in 2001. All isolates had levofloxacin MICs of >32 mg/L when tested by Etest and a double mutation in the quinolone resistance-determining region. All isolates had a *parC* Ser79(r)Phe mutation, two isolates had an additional *gyrB* A435(r)Ile mutation, and the third isolate had an additional *gyrA* Ser83(r)Phe mutation.

In contrast, susceptibility rates were low for trimethoprim + sulphamethoxazole (60.5%), tetracycline (79.5%), and the cephalosporins cefprozil, cefpodoxime and cefuroxime (84.1–84.5%). Erythromycin and the newer macrolides (azithromycin and clarithromycin) demonstrated

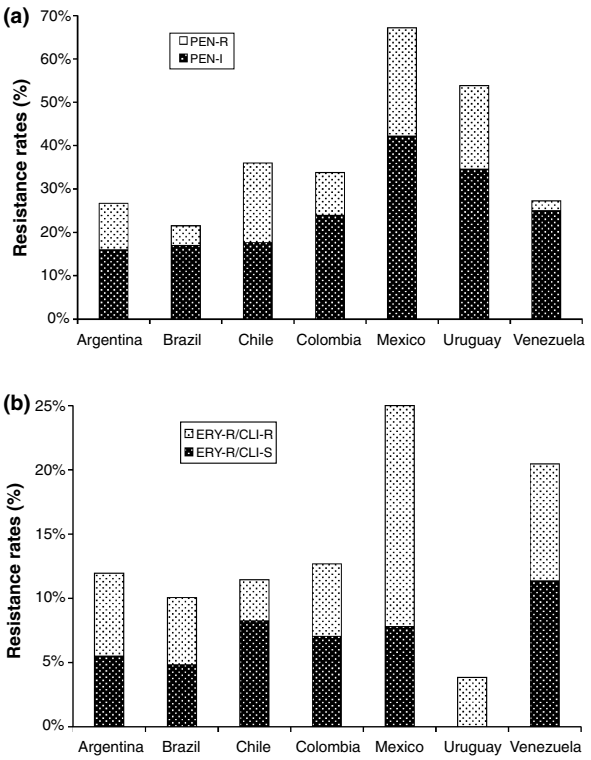

Fig. 1. Rates of resistance of *Streptococcus pneumoniae* to penicillin and erythromycin according to country. Penicillin resistance (a) was divided into intermediate resistance (MIC of 0.12–1 mg/L) and high-level resistance (MIC ≥ 2 mg/L), while erythromycin resistance (b) was divided into *mef* phenotype (resistance to erythromycin and susceptibility to clindamycin) and *erm* phenotype (resistance to both erythromycin and clindamycin).

equivalent antibacterial activity against all isolates, with MIC_{90}s of 2, 2 and 1 mg/L, respectively, and resistance rates of 12.9%, 11.5% and 12.5%.

Penicillin resistance rates (MIC ≥ 2 mg/L) varied from 2.8% in Venezuela to 25.0% in Mexico (Fig. 1a). Comparison of the penicillin resistance rates among Latin American countries revealed some remarkable differences. Most penicillin-non-susceptible isolates from Venezuela and Brazil showed low-level resistance, whereas penicillin-non-susceptible isolates from Argentina and Chile were distributed almost equally in the intermediate and the highly-resistant categories (Fig. 1a). Uruguay (1997 only) and Mexico showed the highest rates of non-susceptible isolates.

The distribution of macrolide resistance rates according to country is shown in Fig. 1b and was similar to that of penicillin resistance, except for Uruguay and Venezuela. However, it is important to note that some countries did not participate for the entire 5-year period and only contributed a small number of isolates. Argentina, Brazil and Chile contributed 86.9% of the isolates, while Colombia, Mexico, Uruguay and Venezuela together contributed only 13.1% of the isolates. Thus, the results from these countries should be analysed with caution.

Rates of resistance to penicillin (MIC ≥ 2 mg/L) and erythromycin (MIC ≥ 1 mg/L) were very similar throughout the years (Fig. 2). The lowest penicillin resistance rate was 9.5% in 1997, while the highest was 13.5% in 1999 (p 0.339).

The in-vitro activity of antimicrobial agents was also evaluated according to the penicillin susceptibility category of the isolates (Table 2). Against penicillin-susceptible *S. pneumoniae* isolates, all β-lactam compounds demonstrated excellent in-vitro activity, and susceptibility rates were very high, except for cefaclor (89.6% susceptibility). As expected, rates of susceptibility to other β-lactam

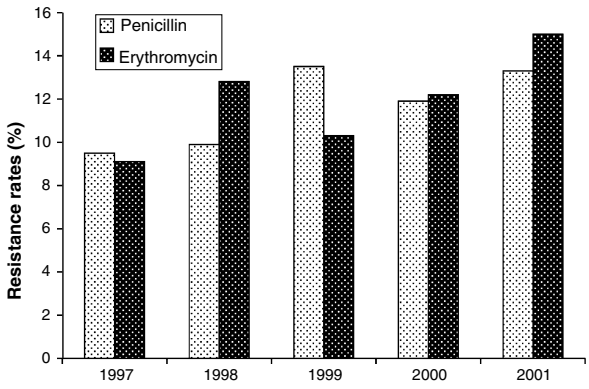

Fig. 2. Penicillin and erythromycin resistance rates according to the year of isolation.

Table 2. In-vitro antimicrobial susceptibilities of penicillin-susceptible, -intermediate and -resistant *Streptococcus pneumoniae* isolates according to their susceptibility to penicillin

	Category (no. of isolates)					
	Penicillin-susceptible (1082)		Penicillin-intermediate (293)		Penicillin-resistant (186)	
Antimicrobial agent	$MIC_{50/90}$	% Susceptible[a]	$MIC_{50/90}$	% Susceptible[a]	$MIC_{50/90}$	% Susceptible[a]
Cefaclor	1/2	89.6	2/32	45.2	> 32/> 32	0.0
Cefuroxime[b]	≤ 0.06/0.12	99.1	0.5/2	67.1	8/8	0.8
Cefprozil	0.25/0.5	99.7	1/8	77.6	16/16	0.0
Cefpodoxime	≤ 0.03/0.06	99.7	0.25/1	80.0	2/4	0.8
Cefotaxime[c]	0.015/0.03	99.8	0.12/0.5	99.0	1/2	87.5
Cefepime	≤ 0.06/0.12	99.9	0.12/0.5	99.3	1/2	80.5
Amoxycillin	≤ 0.06/≤ 0.06	100.0	0.12/1	100.0	2/4	83.8
Erythromycin	0.25/0.25	92.1	0.5/8	80.6	0.25/8	68.1
Azithromycin	≤ 0.12/≤ 0.12	93.0	≤ 0.12/> 16	82.9	≤ 0.12/> 16	71.5
Clarithromycin	≤ 0.25/≤ 0.25	92.6	≤ 0.25/4	81.3	≤ 0.25/16	67.9
Clindamycin	≤ 0.06/0.25	96.6	≤ 0.06/1	89.1	0.12/2	88.6
Gatifloxacin	0.25/0.5	> 99.9	0.25/0.5	100.0	0.25/0.5	98.9
Levofloxacin	1/1	> 99.9	1/1	100.0	1/1	98.9
Chloramphenicol	≤ 2/4	98.0	≤ 2/4	94.2	4/16	83.8
Tetracycline	≤ 2/16	80.2	≤ 2/> 16	75.9	≤ 2/> 16	81.1
Linezolid	1/1	100.0	1/1	100.0	1/2	100.0
Trimethoprim + sulphamethoxazole	0.5/> 1	74.2	> 1/> 1	44.8	> 1/> 1	5.5
Quinupristin + dalfopristin	0.5/0.5	100.0	0.5/1	100.0	0.5/0.5	100.0
Vancomycin	0.25/0.5	100.0	0.5/0.5	100.0	0.5/0.5	100.0

[a]Interpreted by criteria for non-meningitis isolates [9].
[b]Percentage of susceptibility defined by cefuroxime axetil (oral) [9].
[c]Also indicates susceptibility spectrum of ceftriaxone [9].

Table 3. In-vitro antimicrobial susceptibility of isolates collected in medical centres participating in the SENTRY Antimicrobial Surveillance Program (1997–2001)[a]

	Argentina (n = 326)		Brazil (n = 497)		Chile (n = 533)		Latin America total (n = 1561)	
Antimicrobial agent	**$MIC_{50/90}$**	**% Susceptible[b]**	**$MIC_{50/90}$**	**% Susceptible[b]**	**$MIC_{50/90}$**	**% Susceptible[b]**	**$MIC_{50/90}$**	**% Susceptible[b]**
Cefaclor	1/> 32	61.6	1/2	79.7	1/> 32	64.4	1/> 32	68.2
Cefuroxime[c]	≤ 0.06/4	86.5	≤ 0.06/0.5	93.5	≤ 0.06/8	76.8	≤ 0.06/4	81.3
Cefprozil	0.25/8	85.7	0.25/1	93.1	0.25/16	77.4	0.25/8	84.1
Cefpodoxime	≤ 0.03/1	86.9	≤ 0.03/0.25	93.8	0.06/2	76.5	≤ 0.03/2	84.4
Cefotaxime[d]	0.03/0.25	98.2	0.03/0.12	98.6	0.03/1	98.2	0.03/1	98.3
Cefepime	≤ 0.06/1	97.5	≤ 0.06/0.25	99.2	0.12/1	97.0	≤ 0.06/1	97.5
Amoxycillin	≤ 0.06/1	100.0	≤ 0.06/0.12	98.8	≤ 0.06/2	97.8	≤ 0.06/1	98.2
Erythromycin	0.25/1	86.5	0.25/1	88.5	0.25/4	88.0	0.25/2	87.1
Azithromycin	≤ 0.12/0.5	90.0	≤ 0.12/0.5	91.4	≤ 0.12/2	86.7	≤ 0.12/2	88.5
Clarithromycin	≤ 0.25/0.5	88.1	≤ 0.25/0.5	89.2	≤ 0.25/2	87.2	≤ 0.25/1	87.5
Clindamycin	≤ 0.06/0.25	93.3	0.12/0.25	94.6	≤ 0.06/0.25	96.6	≤ 0.06/0.25	94.5
Gatifloxacin	0.25/0.5	99.4	0.25/0.5	100.0	0.25/0.5	99.6	0.25/0.5	99.8
Levofloxacin	1/1	99.6	1/1	100.0	1/1	99.6	1/1	99.8
Chloramphenicol	≤ 2/4	93.3	≤ 2/4	98.2	≤ 2/4	97.6	≤ 2/4	95.6
Tetracycline	≤ 2/> 16	82.2[e]	≤ 2/> 16	80.5[e]	≤ 2/> 16	84.4[e]	≤ 2/> 16	81.0[e]
Linezolid	1/1	100.0	1/1	100.0	1/2	100.0	1/1	100.0
Trimethoprim + sulphamethoxazole	≤ 0.5/> 1	70.6	0.5/> 1	49.7	≤ 0.5/> 1	62.0	0.5/> 1	60.5
Quinupristin + dalfopristin	0.5/0.5	100.0	0.5/0.5	100.0	0.5/0.5	100.0	0.5/0.5	100.0
Vancomycin	0.25/0.5	100.0	0.25/0.5	100.0	0.25/0.5	100.0	0.25/0.5	100.0

[a]Only countries with more than 300 isolates are included individually in the table.
[b]Interpreted according to criteria for non-menigitis isolates [9].
[c]Percentage of susceptibility defined by cefuroxime axetil (oral) [9].
[d]Also indicates susceptibility spectrum of ceftriaxone [9].
[e]Includes susceptible and intermediate isolates.

agents were relatively low (0–87.5%) among penicillin-resistant isolates. Trimethoprim + sulphamethoxazole showed the lowest susceptibility rates (60.5%), which varied from 74.2% among penicillin-susceptible strains to 5.5% among strains highly resistant to penicillin (Tables 1 and 2). Linezolid, vancomycin and quinupristin + dalfopristin were the most active compounds overall (100% susceptibility), followed by the fluoroquinolones gatifloxacin and levofloxacin with 99.8% susceptibility (Tables 1 and 3).

Resistance rates for non-β-lactam drugs were also higher among penicillin-resistant strains than among penicillin-susceptible strains. As shown in Table 2, resistance to fluoroquinolones was not affected by the susceptibility to penicillin. Chloramphenicol resistance was more frequent among isolates highly resistant to penicillin (16.2%) than among strains with low-level resistance (2.0%). This correlation with penicillin resistance categories was not observed for tetracycline, where around 20% of isolates were resistant regardless of their penicillin susceptibility category.

Comparison of the susceptibility rates among countries showed striking differences (Table 3). Higher rates of resistance were observed in Mexico compared to Argentina, Brazil and Chile. In addition, the Brazilian centres showed trimethoprim + sulphamethoxazole susceptibility rates (49.7%) that were significantly lower than those of either the Argentinean or Chilean centres (49.7% vs. 70.6% and 62.0%, respectively; $p < 0.001$).

Twenty-three erythromycin-resistant strains were screened by molecular methods for *ermB* and *mefA* genes. Ten (43.5%) strains were positive for *ermB* and 13 (56.5%) strains were positive for *mefA*.

DISCUSSION

An increasing prevalence of penicillin-resistant pneumococci has been identified throughout the world. In Latin America, the prevalence of penicillin resistance among clinical isolates of pneumococci has also been evaluated by the Sistema Regional de Vacunas Project [11]. This programme was conducted by the Pan-American Health Organization and, similar to the findings of the present study, its results have shown that penicillin resistance rates varied markedly according to country.

Although recent reports from Latin America [1,2,12] have demonstrated an increase in penicillin resistance rates, the results of the present study showed stable rates of penicillin susceptibility throughout the period evaluated. High rates of resistance to other β-lactam agents were expected in penicillin-non-susceptible strains, since it is well-documented that the mechanism of resist-

ance to β-lactam agents is altered penicillin-binding proteins [13]. The difference between pneumococci susceptibility rates for penicillin and amoxycillin is explained by differences in the susceptibility breakpoints (≤ 0.06 mg/L for penicillin and ≤2 mg/L for amoxycillin), since both β-lactam compounds have similar activity *in vitro* against this pathogen [9].

Cefotaxime resistance was found in 0.4% of isolates; however, only two isolates were from blood, while the others were isolated from the respiratory tract. These strains were isolated from different Latin American countries during 1997–1999. Strains highly resistant to penicillin showed a tendency to be more resistant to some antimicrobial agents, including non-β-lactam compounds. The reasons for cross-resistance to several antimicrobial classes are not completely understood, but some resistant determinants are carried on the same mobile genetic elements [2].

Despite the mechanisms of resistance to macrolides being completely distinct from those causing β-lactam resistance, penicillin-non-susceptible *S. pneumoniae* isolates are usually less susceptible to this agent [1]. Macrolide resistance in *S. pneumoniae* may be caused by two distinct mechanisms of resistance: (1) target-site modification by methylation of the 23S ribosomal RNA; and (2) efflux of the antibiotic, associated with expression of the *mefE* gene. Ribosomal methylation, encoded by the *erm* gene, leads to cross-resistance to macrolides, lincosamides (clindamycin) and streptogramin B, the so-called MLS_B phenotype. The efflux mechanism is caused by an inducible expressed pump that confers resistance only to macrolides. Based on the clindamycin results, 42.5% of erythromycin-resistant strains appeared to carry the MLS_B phenotype, while 57.5% seemed to possess the efflux mechanism. The molecular analysis performed on the isolates collected in 2001 confirmed these results, since 43.5% of isolates were positive for *ermB* and 56.5% were positive for *mefA*. On the other hand, these results are in contrast to those obtained by the Sistema Regional de Vacunas Project, which showed that MLS_B was the most common macrolide resistance phenotype [12].

Other investigators [1,12,14,15] have also reported elevated rates of resistance to tetracycline and trimethoprim + sulphamethoxazole in Latin American countries. The low cost and easy access to these drugs recommended by the World Health Organisation may, in part, explain these higher rates of resistance. On the other hand, chloramphenicol showed an excellent spectrum against Latin American pneumococcal isolates (95.6% susceptibility overall).

Fluoroquinolones with enhanced anti-pneumococcal activity (e.g., gatifloxacin and levofloxacin) represent attractive antimicrobial treatment options for community-acquired respiratory infections in adults [16,17]. Currently, resistance to these fluoroquinolones (gatifloxacin and levofloxacin) is very rare in Latin American isolates (< 1%) [1,14,15]. The present study found three isolates (0.19%) resistant to both gatifloxacin and levofloxacin. These strains were from Chile (two isolates) and Argentina (one isolate), and all three had a double mutation in the quinolone resistance-determining region. Resistance to vancomycin, linezolid and quinupristin + dalfopristin was not observed. These drugs and the fluoroquinolones were the most active compounds against penicillin-resistant *S. pneumoniae*.

Several surveillance programmes have evaluated the antimicrobial susceptibility of *S. pneumoniae* in the last few years. However, the number of isolates from the Latin America region is usually low. The present study tested a large number of isolates against most antimicrobial agents currently used to treat pneumococcal infections. The results highlighted the main resistance problems and showed that resistance rates may vary significantly among regions and also within a geographical region. It is important to note that the study collected isolates from a limited number of centres in a very large and diverse geographical area. Thus, the results may not reflect the resistance rates in other countries of the region, or in other regions of the countries evaluated.

REFERENCES

1. Hoban DJ, Doern GV, Fluit AC, Roussel-Delvallez M, Jones RN. Worldwide prevalence of antimicrobial resistance in *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* in the SENTRY Antimicrobial Surveillance Program, 1997–1999. *Clin Infect Dis* 2001; **32**(suppl 2): S81–S93.
2. Appelbaum PC. Resistance among *Streptococcus pneumoniae*: implications for drug selection. *Clin Infect Dis* 2002; **34**: 1613–1620.
3. Metlay JP, Singer DE. Outcomes in lower respiratory tract infections and the impact of antimicrobial drug resistance. *Clin Microbiol Infect* 2002; **8**(suppl 2): 1–11.

4. Gales A, Sader H, Jones RN. Activities of BMS 284756 (T-3811) against *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae* isolates from SENTRY antimicrobial surveillance program medical centers in Latin America (1999). *Antimicrob Agents Chemother* 2001; **45**: 1463–1466.
5. Sneed JO. Processing and interpretation of respiratory tract specimens. In: Isenberg HD, ed. *Clinical microbiology procedures handbook*, Vol. 1. Washington, DC. American Society for Microbiology, 1992; 1.15.1–1.15.8.
6. Farrell DJ, Morrisey I, Bakker G, Felmingham D. Detection of macrolide resistance mechanisms in *Streptococcus pneumoniae* and *Streptococcus pyogenes* using a multiplex rapid cycle PCR with microwell-format probe hybridization. *J Antimicrob Chemother* 2001; **48**: 541–544.
7. Ruoff KL, Whiley RA, Beighton D. *Streptococcus*. In: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. *Manual of clinical microbiology*, 7th edn. Washington, DC: ASM Press, 1999; 283–296.
8. National Committee for Clinical Laboratory Standards. *Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically*, 6th edn. Approved document M7-A5. Wayne, PA: NCCLS, 2003.
9. National Committee for Clinical Laboratory Standards. *Performance standards for antimicrobial susceptibility testing, twelfth Informational Supplement*. M100-S13. Wayne, PA: NCCLS, 2003.
10. Gales AC, Gordon KA, Wilke WW, Pfaller MA, Jones RN. Occurrence of single-point *gyrA* mutations among ciprofloxacin-susceptible *Escherichia coli* isolates causing urinary tract infections in Latin America. *Diagn Microbiol Infect Dis* 2000; **36**: 61–64.
11. Di Fabio JL, Castaneda E, Agudelo CI *et al*. Evolution of *Streptococcus pneumoniae* serotypes and penicillin susceptibility in Latin America, Sireva-Vigia Group, 1993 to 1999. PAHO Sireva-Vigia Study Group. Pan American Health Organization. *Pediatr Infect Dis J* 2001; **20**: 959–967.
12. Tomasz A, Corso A, Severina EP *et al*. Molecular epidemiologic characterization of penicillin-resistant *Streptococcus pneumoniae* invasive pediatric isolates recovered in six Latin-American countries: an overview. *Microb Drug Resist* 1998; **4**: 195–207.
13. Hakenbeck R, Kaminski K, Konig A *et al*. Penicillin-binding proteins in beta-lactam-resistant *Streptococcus pneumoniae*. *Microb Drug Resist* 1999; **5**: 91–99.
14. Critchley IA, Thornsberry C, Hickey ML *et al*. Antimicrobial susceptibility of *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* collected from five centers in Brazil, 1998. *Clin Microbiol Infect* 2000; **6**: 178–184.
15. Sader HS, Gales AC, Granacher TL, Pfaller MA, Jones RN. Prevalence of antimicrobial resistance among respiratory tract isolates in Latin America: results from SENTRY Antimicrobial Surveillance Program (1997–98). *Braz J Infect Dis* 2000; **4**: 245–254.
16. Jones RN. Microbiology of newer fluoroquinolones: focus on respiratory pathogens. *Diagn Microbiol Infect Dis* 2002; **44**: 213–220.
17. Zhanel GG, Ennis K, Vercaigne L *et al*. A critical review of the fluoroquinolones: focus on respiratory infections. *Drugs* 2002; **62**: 13–59.